

*Amendments to the Claims*

The claims have been amended to more particularly point out and distinctly claim the present invention. In particular, claims 10 and 11 have been canceled. Claim 20 has been added and is supported by the specification at, for example, page 9, lines 21-29. No new matter has been added by way of these amendments. The precise changes to the claims and the pending claims, as amended, are set forth on an attachments hereto.

*Summary of the Office Action*

Claims 1-19 are rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent 4,136,193 (Bogeso et al.) in combination with Carré ("Précis de Technologie et de Chimie Industrielle," volume 1, pp. 319-320 (Librairie J.-B. Baillière et Fils, Paris, France, 1938)).

*Discussion of the Obviousness Rejection*

According to the Office Action, the Examiner contends that Bogeso et al. teaches citalopram derivatives of the type recited in the pending claims. The Examiner concedes that Bogeso et al. fails to specify the claimed particle size; however, the Examiner asserts that it would have been obvious to rely on the teachings of Carré in order to modify the citalopram derivative of Bogeso et al. and arrive at the present invention. Carré allegedly discloses modifying reaction parameters such as temperature and the rate of cooling to produce particles of a given size and uniformity.

Bogeso et al. discloses the production of citalopram hydrobromide by a conventional method (col. 5, line 67, through col. 6, line 8). Bogeso et al. does not, however, disclose the particle size or average aspect ratio of the citalopram hydrobromide, which are required elements of the present invention, as defined by claims 1-8. Carré discloses a method for controlling the size of a crystal. In particular, Carré teaches that (a) by placing an agitator in the solution-containing recipient or by shaking the entire recipient, crystals of small size can be obtained, (b) crystals with a more homogeneous size can be prepared by using crystallizers that have an oscillating or rocking movement, and (c) cooling crystals quickly results in smaller crystals (see third paragraph of the English translation).

The present invention, as defined by claims 1-5, requires that, at most, 35% of citalopram hydrobromide crystals have a particle size of less than 5  $\mu\text{m}$ . The Examiner concedes that Bogeso et al. does not disclose any particle size of citalopram hydrobromide crystals, let alone citalopram hydrobromide crystals in which at most 35% have a particle size of 5  $\mu\text{m}$  or less. However, Carré does not provide these missing elements. Carré does not teach or suggest preparing crystals in which at most 35% have a particle size of 5  $\mu\text{m}$  or less.

At best, Carré teaches general methods of obtaining crystals of "small size" or preparing crystals with a more homogeneous size by using crystallizers that have an oscillating or rocking movement. These methods do not particularly relate to the present invention, since Carré does not provide any definition of, or associate a particular size with, the phrase "small size." In addition, citalopram hydrobromide crystals, of which at most 35% have a particle size of 5  $\mu\text{m}$  or less, are not necessarily of a homogeneous size since 65% of the citalopram hydrobromide crystals can have a particle size greater than 5  $\mu\text{m}$ . Therefore, if the disclosures of the two references were combined, one of ordinary skill in the art still would not end up with the present invention. Carré does not provide teachings that would enable the ordinarily skilled artisan to arrive at the present invention, as defined by claims 1-5. The ordinarily skilled artisan would have no idea what temperature ranges or cooling rates to use that would enable the preparation of citalopram hydrobromide crystals of which at most 35% have a particle size of 5  $\mu\text{m}$  or less.

Moreover, neither Bogeso et al. nor Carré teaches anything about an average aspect ratio. Specifically, neither reference teaches citalopram hydrobromide crystals with a specific average aspect ratio. Therefore, the combination of Bogeso et al. and Carré does not teach all of the elements of the present invention, as defined by claims 6-8. The average aspect ratio of a crystal relates to its overall shape and is measured as the ratio of the length of the crystal to its width. For example, a crystal with an average aspect ratio of 1 (i.e., 1:1) is perfectly spherical. As discussed above, Carré only generally teaches preparing crystals of a small or homogeneous size, which is distinctly different from preparing a crystal of a given average aspect ratio. A small or homogeneous size has nothing to do with a crystal's shape. Upon reading the disclosure of Carré, one of ordinary skill in the art would not glean any teaching or suggestion of how to prepare a crystal of any average aspect ratio, let alone citalopram hydrobromide with an average aspect ratio of, for example, not less than 2.0 and not more than 9.0.

Regarding claims 9 and 12-20, the combination of Bogeso et al. and Carré does not render the present invention obvious. Bogeso teaches preparing citalopram hydrobromide by a "conventional manner" and does not disclose cooling the citalopram hydrobromide to allow for crystallization while controlling the cooling rate. Carré does not provide the missing teaching since Carré only states that "the quicker the cooling, the smaller the crystals." This teaching is not equivalent to controlling the cooling rate, and could, if anything, be interpreted as implying that the rate itself does not matter, just as long as the solution is cooled quickly. The two methods are not synonymous. Therefore, even if the disclosures of Bogeso et al. and Carré were combined, one would not arrive at the present invention as defined by claims 9 and 12-20.

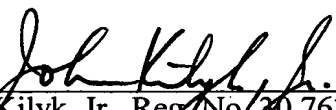
In re Appln. of Ikemoto et al.  
Application No. 09/824,447

Without a teaching or suggestion of all the elements of the present invention, pending claims 1-20 must be considered to define unobvious subject matter in view of the disclosures of Bogeso et al. and Carré. Accordingly, applicants request that the rejection be withdrawn.

*Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

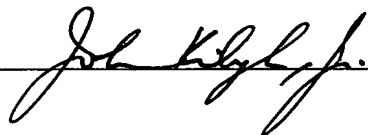
  
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Date: November 18, 2002

**CERTIFICATE OF MAILING**

I hereby certify that this RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Date: November 18, 2002

  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Ikemoto et al.

Art Unit: 1625

Application No. 09/824,447

Examiner: R. K. Covington

Filed: April 2, 2001

For: CITALOPRAM HYDROBROMIDE  
CRYSTAL AND METHOD FOR  
CRYSTALLIZATION THEREOF

AMENDMENTS TO CLAIMS  
MADE IN RESPONSE TO OFFICE ACTION DATED AUGUST 19, 2002

*(Deletions are indicated by cross-out text,  
while insertions are indicated by underlined text)*

10. (Canceled)

11. (Canceled)

20. (New) The method of claim 12, which comprises, after cooling to a temperature range of from not less than 30°C to less than 48°C, adding a seed crystal of citalopram hydrobromide for crystallization.